REMARKS

Claims 1-43, 50-55 and 61 are pending in this application. By this amendment, applicants have amended claim 1 and added new claims 62-66. Applicants have also canceled claim 2 without disclaimer or prejudice to applicants' rights to pursue the subject matter of this claim in this or another application. Accordingly, claims 1, 3-43, 50-55 and 61-66 are pending in this application.

Support for the amendment to claim 1 may be found, *inter alia*, on page 37, lines 25-27 of the subject specification.

Support for new claim 62 may be found, *inter alia*, on page 8, line 5 of the subject specification.

Support for new claim 63 may be found, *inter alia*, on page 8, lines 5-7 of the subject specification.

Support for new claim 64 may be found, *inter alia*, on page 9, line 22 of the subject specification.

Support for new claim 65 may be found, *inter alia*, on page 9, lines 22-23 of the subject specification.

Support for new claim 66 may be found, *inter alia*, on page 9, lines 23-24 of the subject specification.

Species Election

The Examiner acknowledged applicants' timely election with traverse of Group I, claims 1-43, 50-55 and 61. The Examiner also acknowledged applicants' timely election with traverse of

the species, a pharmaceutical composition in a solid form such as a tablet recited in claim 24.

The Examiner stated that claims 1 and 23-24 read on the elected species. The Examiner withdrew claim 55 from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there allegedly being no allowable generic or linking claim. The Examiner also withdrew claims 2-22, 25-43, 50-54 and 61, which allegedly read on the non-elected species, alleging that art was found on the elected species.

In response, applicants contend that the Examiner's withdrawal of claims 2-22, 25-35, 39, 43, 50-54 and 61 was improper. The Examiner alleged that only "Claims 1 and 23-24 read on the elected species." This is not true. Pursuant to MPEP §806.04(f), "Claims to be restricted to different species must be mutually exclusive." Claim 24 is directed to a pharmaceutical composition comprising a therapeutically effective amount of Copolymer 1 (glatiramer acetate) and microcrystalline cellulose in solid form, which is <u>not</u> mutually exclusive of the amount of microcrystalline cellulose in the composition by weight recited in claims 2-5, or of the moisture content of the microcrystalline cellulose in the pharmaceutical composition recited in claims 6-7. Similarly, the elected solid form species recited in claim 24 is <u>not</u> mutually exclusive of the disintegrant recited in claims 8-10, or of the moisture content of the disintegrant recited in claims 11-14, or of the lubricant recited in claims 16-17, or of the enteric coating recited in claims 18-20, or the film coating recited in claims 21-22, or the pharmaceutically acceptable carrier suitable for application to the mucosal linings of a subject recited in claims 32-33, or the anti-

microbial preservative recited in claims 34-35, or the protease inhibitor recited in claim 61.

The elected solid form species recited in claim 24 is also not mutually exclusive of the tablet comprising specific amounts of Copolymer 1 recited in claims 25-28. Additionally, the elected solid form species recited in claim 24 is not mutually exclusive of the solid form comprising an amount of Copolymer 1, a percentage by weight of microcrystalline cellulose and an enteric coating recited in claims 29-31 and 50-54. Also, the solid form species recited in claim 24 is not mutually exclusive of the oral form recited in claim 39. Similarly, the elected solid form species recited in claim 24 is not mutually exclusive of the process of its manufacture recited in claim 43.

Accordingly, claims 2-22, 25-35, 39, 43, 50-54, and 61 read on the elected solid form species of a tablet recited in claim 24 and should not have been withdrawn. Therefore, applicants respectfully request that the Examiner rejoin claims 2-22, 25-35, 39, 43, 50-54, and 61.

Moreover, pursuant to MPEP § 809.02(c), an Examiner's action subsequent to an election of species should include a complete action on the merits of all claims readable on the elected species. However, on page 2 of the December 30, 2002 Office Action, the Examiner alleged, "Since art was found on the elected species, claims 2-22, 25-43, 50-54 and 61, which read on the non-elected species, have been withdrawn from consideration" [emphasis added]. However, claims 1-22, 25-35, 39, 43, 50-54 and 61 read on the elected species, also. Thus, the Examiner erroneously excluded claims which read on both the elected and the non-elected species. This is contrary to

MPEP § 809.02(c), which required "a complete action on the merits of all claims readable on the elected species" [emphasis added], and permits withdrawal of only claims "not readable on the elected species."

Information Disclosure Statement

On pages 2-3 of the December 30, 2002 Office Action, the Examiner noted that applicants filed an Information Disclosure Statement and accompanying references on July 8, 2002 (Paper No. 7). However, the Examiner indicated that the PTO-1449 Form and said references are not able to be located by the Examiner. The Examiner requested that applicants send a courtesy copy of said PTO-1449 Form and paper copies of the references listed therein.

In accordance with the Examiner's request, applicants attach hereto a courtesy copy of the Information Disclosure Statement and copies of the references mailed on July 2, 2002 and received by the U.S. Patent and Trademark Office on July 8, 2002, as evidenced by the copy of the stamped postcard receipt attached hereto as **Exhibit 2**.

Claim Rejections under 35 U.S.C. § 103

On page 3 of the December 30, 2002 Office Action, the Examiner rejected claims 1 and 23-24 under 35 U.S.C. § 103(a) as allegedly unpatentable over PCT International Publication No. WO 98/30227, in view of US Patent 3,991,210.

The Examiner alleged that '227 teaches a pharmaceutical composition comprising as an active ingredient a therapeutically effective amount of Copolymer 1 (glatiramer

acetate). The Examiner also alleged that '227 teaches a method of treating multiple sclerosis by oral administration of copolymer-1 through ingestion, and that when copolymer-1 is introduced orally, it may be in solid form, and it may be mixed with a pharmaceutically acceptable carrier.

The Examiner acknowledged that '227 does not specifically teach that said carrier is microcrystalline cellulose.

The Examiner alleged that '210 teaches that microcrystalline cellulose is a solid pharmaceutical carrier for solid compositions such as tablets, citing the entire patent, especially column 3, last paragraph and column 4, lines 1-2, and that tablets allegedly can be made in unit dosage forms adapted for oral administration, citing column 4, lines 30-35.

Therefore, the Examiner alleged that one of skill who wanted to treat a patient with multiple sclerosis would have been motivated to make a solid form of a pharmaceutical composition comprising as an active ingredient, a therapeutically effective amount of Copolymer 1, as allegedly taught by '227, wherein said solid form was a tablet comprising microcrystalline cellulose as allegedly taught by '210, because '227 teaches that multiple sclerosis can be treated by oral administration of Copolymer 1, and because '210 allegedly teaches that tablets can be made for oral administration, and that microcrystalline cellulose is allegedly an acceptable solid pharmaceutical carrier for solid compositions such as tablets.

The Examiner alleged that, from the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in

producing the claimed invention. Therefore, the Examiner alleged that the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

In response, applicants have amended claim 1 to recite "an amount of microcrystalline cellulose in excess of 50 % by weight of the composition." Applicants assert that neither of the cited references teach or suggest that the pharmaceutical composition comprise in excess of 50 % microcrystalline cellulose by weight. As disclosed on page 37, line 17 to page 38, line 13, use of in excess of 50 % microcrystalline cellulose by weight

> results in pharmaceutical compositions with excellent flow and mixing characteristics, improved dissolution and improved stability than that which could have been expected based on the properties of Copolymer 1.
>
> Indeed, based on the properties of Copolymer 1, it was unexpected that the formulation with microcrystalline cellulose, particularly in excess of 50 %, would have significantly improved pharmaceutical properties suitable for oral administration.
>
> The advantageous properties of the disclosed formulation include that it allows for matching *in vitro* dissolution profiles of the 5 mg Copolymer 1 and the 50 mg Copolymer 1 tablets weight as shown in Figure 3. Specifically, and unexpectedly, even though the 50 mg Copolymer 1 tablet is four times the weight of the 5 mg Copolymer 1 tablet the tablets have similar dissolution profiles. (page 37, line 29 to page 38, line 13).

Thus, it is unexpected that the use of in excess of 50 % by

weight microcrystalline cellulose will produce such advantageous properties in the pharmaceutical compositions of the subject invention.

Furthermore, although '210 includes microcrystalline cellulose in a laundry list of solid pharmaceutical carriers in column 3, line 67 to column 4, line 2, there is no motivation for one of skill in the art to select applicants' particular carrier, microcrystalline cellulose. As the above-quoted section of the subject specification establishes, the use of microcrystalline cellulose, particularly when in excess of 50% by weight of the pharmaceutical composition, imparts superior and unexpected characteristics to applicants' pharmaceutical compositions.

For all of the above reasons, applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. §103.

FOURTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT PURSUANT TO 37 C.F.R. §1.97(c)(2)

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following publication which is listed again on the attached Form PTO-1449 **(Exhibit 3)** and a copy of Reference 1 **(Exhibit 4)** is enclosed.

This Fourth Supplemental Information Disclosure Statement is being submitted after the issuance of a first Office Action on the merits in connection with the subject application, but prior to the issuance of a final action under 37 C.F.R § 1.113, a notice of allowance under 37 C.F.R. § 1.311 or an action that otherwise closes prosecution. Pursuant to 37 C.F.R. § 1.97(c)(2), the required fee for filing an

Information Disclosure Statement is $180.00 and a check including this amount is enclosed. Accordingly, this Fourth Supplemental Information Disclosure Statement shall be considered pursuant to 37 C.F.R. §1.97(c)(2).

1. U.S. Patent Publication No. US-2002-0107388-A1, published August 8, 2002 (Vandenbark)**(Exhibit 4)**.

Applicants request that the Examiner review the publication and make it of record in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed $290.00 ($180.00 for the Fourth Supplemental Information Disclosure Statement and $110.00 for the one-month extension of time for responding to the December 30, 2003 Office Action), is deemed necessary in connection with the filing of this Amendment and Fourth Supplemental Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given

to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents Washington, D.C. 20231

John P. White 4/30/03

John P. White Date
Reg. No. 28,678